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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/904,553	07/13/2001	Avi Ashkenazi	10466/39	9211

30313 7590 10/01/2002

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EXAMINER
ROMEO, DAVID S

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 10/01/2002 16

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/904,553	ASHKENAZI ET AL.	
	Examiner	Art Unit	
	David S Romeo	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 August 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *39-51* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *44-49* is/are allowed.

6)☒ Claim(s) *39-43,50 and 51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *8* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The preliminary amendments filed August 26, 2002 (Paper No. 7) and concurrently with the present application (Paper No. 9) have been entered. Claims 39-51 are pending and being examined.

According to the priority statement of August 26, 2002 (Paper No. 7), it appears that the claimed subject matter defined in the instant application is supported by the parent application PCT/US00/04414 filed February 22, 2000. Based on the information given by applicant and an inspection of the patent applications, the examiner has concluded that the subject matter defined in this application is supported by the disclosure in application PCT/US00/04414 filed February 22, 2000, but is not supported by any of the others because in order to obtain the benefit of an earlier filing date in the United States under 35 U.S.C. 120 an invention must disclosed in the manner provided by the first paragraph of section 112 of this title in an application previously filed in the United States. The limitation "extracellular domain" is new matter with respect to any of the other applications filed prior to February 22, 2000. Also, prior to February 22, 2000 the PRO214 polypeptide is not supported by either a specific and substantial asserted utility or a well established utility, and one skilled in the art clearly would not know how to use the claimed invention. Accordingly, the subject matter defined in claims 39-51 has an effective filing date of February 22, 2000.

Should the applicant disagree with the examiner's factual determination above, it is incumbent upon the applicant to provide the serial number and specific page number(s) of any parent application filed prior to February 22, 2000 which specifically supports the particular

claim limitation for each and every claim limitation in all the pending claims which applicant considers to have been in possession of and fully enabled for prior to February 22, 2000.

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. For example, see page 69, line 8. This list is not meant to be exhaustive. The lengthy specification has not been checked to the extent necessary to determine the presence of all embedded hyperlinks and/or other forms of browser-executable code. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

The application is not fully in compliance with the sequence rules, 37 C.F.R. § 1.821-1.825. Specifically, the specification fails to recite the appropriate sequence identifiers at each place where a sequence is discussed. See page 14, line 17. This is not meant to be an exhaustive list of places where the specification fails to comply with the sequence rules. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification. The application cannot issue until it is in compliance. Nucleic acid sequences with 10 or more nucleotides, at least 4 of which are specifically defined, must comply with the sequence rules. Amino acid sequences with 4 or more residues, at least 4 of which are specifically defined, must comply with the sequence rules. Sequence identifiers can

also be used to discuss and/or claim parts or fragments of a properly presented sequence. For example, language such as "residues 14 to 243 of SEQ ID NO:23" is permissible and the fragment need not be separately presented in the "Sequence Listing."

Correction is required.

Information Disclosure Statement

The sequences in the information disclosure statement filed March 14, 2002 have been considered to the extent possible, but a residue by residue comparison has not been done. The "Other Art" will not be listed on any patent resulting from this application because it was not provided on a separate list in compliance with 37 CFR 1.98(a)(1). In order to have the references printed on such resulting patent, a separate listing, preferably on a PTO-1449 or PTO/SB/08A and 08B form, must be filed within the set period for reply to this Office action.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 39-43, 50, 51 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated polypeptide comprising an amino acid sequence at least 80% identical an amino acid sequence selected from the group consisting of the amino acid sequence of SEQ ID NO: 109, the amino acid sequence of SEQ ID NO: 109 lacking the associated signal peptide, the amino acid sequence of the extracellular domain of the amino

acid sequence of SEQ ID NO: 109, and the amino acid sequence of the extracellular domain of the amino acid sequence of SEQ ID NO: 109 lacking the associated signal peptide, wherein said isolated polypeptide inhibits vascular endothelial growth factor (VEGF) stimulated proliferation of endothelial cell growth, does not reasonably provide enablement for said isolated polypeptide without regard to the functional activity thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is undue include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The claims are drawn to a polypeptide having at least 80% amino acid sequence identity to the polypeptide of SEQ ID NO: 109, referred to as PRO214, or to some portion thereof. There is no functional limitation in the claims. Applicants have taught that PRO214 inhibits vascular endothelial growth factor (VEGF) stimulated proliferation of endothelial cell growth (Example 66, page 204).

The claim encompasses an unreasonable number of inoperative polypeptides, which the skilled artisan would not know how to use. While the specification suggests that PRO214 is a member of the family comprising EGF domains and may posses properties typical of the EGF-domain containing family, it is unclear what properties polypeptides 80% identical to PRO214

may possess. While it is accepted in the art that EGF-like domains mediate protein-protein interactions (Campbell (u10), paragraph bridging pages 385-386; Appella (v10), page 2, column 1, full paragraph 2), the prior art of Campbell (u10) teaches that the functions of EGF-like domain containing proteins are diverse, ranging from growth factors, to extracellular matrix proteins, to cell membrane receptors (page 386, column 1). The prior art of Bender (w10) teaches that many mammalian proteins contain EGF-like homology units but that it is difficult to define a common function for all of them (page 560, column 1, full paragraph 3). The prior art of Lecka-Czernick (x10) teaches that a single point mutation in which changes only a single conserved amino acid in the EGF-like domain of fibrillin and factor IX abolishes the proteins' functional activity (page 125, paragraph bridging columns 1-2). The prior art of Engel (y10) teaches that a single point mutation in one of the 35 EGF-like repeats of Notch has dramatic effects on its biological activity (paragraph bridging pages 5-6). Therefore, knowledge of one EGF-domain containing polypeptide's structure and function does not provide predictability about function of a structurally related polypeptide, even within the same class.

There are no working examples of polypeptides less than 100% identical to PRO214. The skilled artisan would not know how to use non-identical polypeptides on the basis of teachings in the prior art or specification unless they inhibited vascular endothelial growth factor (VEGF) stimulated proliferation of endothelial cell growth. The specification does not provide guidance for using polypeptides related to (i.e., 80%-99% identity) but not identical to PRO214 which do not have a single specific disclosed activity show for PRO214. The claims are broad because they do not require the claimed polypeptide to be identical to the disclosed sequence and because the claims have no functional limitation.

For these reasons, which include the complexity and unpredictability of the nature of the invention and art in terms of the diversity of EGF-domain containing polypeptides and lack of knowledge about function(s) of encompassed polypeptides structurally related to PRO214, the lack of direction or guidance for using polypeptides that are not identical to PRO214, and the breadth of the claims encompassing structure without function, it would require undue experimentation to use the invention commensurate in scope with the claims.

Claims 39-43, 50, 51 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to polypeptides having at least 80%, 85%, 90%, 95% or 99% sequence identity with a particular disclosed sequence. The claims do not require that the polypeptide possess any particular biological activity, nor any particular conserved structure, or other disclosed distinguishing feature. Thus, the claims are drawn to a genus of polypeptides that is defined only by sequence identity.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a partial structure in the form of a recitation of percent identity. There is no recitation of a

structure/function correlation. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See Fiers v. Revel, 25 USPQ2d 1601 at 1606 (CAFC 1993) and Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481 at 1483. In Fiddes, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only isolated polypeptides comprising the amino acid sequence set forth in SEQ ID NO: 109, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that Vas-Cath makes clear that the

written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

The following rejection under 35 U.S.C. § 102 is made under the assumption that the effective filing date for the instantly claimed invention is February 22, 2000.

Claims 39-42, 50, 51 are rejected under 35 U.S.C. 102(a) as being anticipated by Ruben (n10). Ruben discloses an isolated polypeptide (page 185, lines 16-17) comprising the amino acid sequence of SEQ ID NO: 138 (page 59, line 29, through page 62, line 6; page 175; page 288, claim 11; pages 88-89 of the sequence listing). Ruben also discloses the signal peptide of SEQ ID NO: 138, comprising amino acids 1-26 of SEQ ID NO: 138 (page 175; page 185, line 26, through page 186, line 25). The amino acid sequence of Ruben's SEQ ID NO: 138 is 97% identical to the amino acid sequence of the polypeptide shown in Figure 40 (SEQ ID NO: 109) of the present application, as indicated below:

```
AAY76151
ID   AAY76151 standard; Protein; 434 AA.
XX
AC   AAY76151;
XX
DT   23-MAR-2000  (first entry)
XX
DE   Human secreted protein encoded by gene 28.
XX
KW   Human; secreted protein; cancer; tumour; developmental abnormality;
KW   foetal deficiency; blood disorder; immune system disorder; inflammation;
KW   autoimmune disease; allergy; Alzheimer's disease; cognitive disorder;
KW   schizophrenia; arthritis; asthma; psoriasis; sepsis; skin disorder;
```

KW atherosclerosis; diabetes; cardiovascular disorder; kidney disorder;
KW digestive disorder; endocrine disorder; infection; AIDS; leukaemia;
KW therapy; chromosome 3.
XX
OS Homo sapiens.
XX
PN WO9958660-A1.
XX
PD 18-NOV-1999.
XX
PF 06-MAY-1999; 99WO-US09847.
XX
PR 12-MAY-1998; 98US-0085093.
PR 12-MAY-1998; 98US-0085094.
PR 12-MAY-1998; 98US-0085105.
PR 12-MAY-1998; 98US-0085180.
PR 18-MAY-1998; 98US-0085906.
PR 18-MAY-1998; 98US-0085920.
PR 18-MAY-1998; 98US-0085921.
PR 18-MAY-1998; 98US-0085922.
PR 18-MAY-1998; 98US-0085923.
PR 18-MAY-1998; 98US-0085924.
PR 18-MAY-1998; 98US-0085928.
PR 18-MAY-1998; 98US-0085925.
PR 18-MAY-1998; 98US-0085927.
XX
PA (HUMA-) HUMAN GENOME SCI INC.
XX
PI Ruben SM, Florence K, Ni J, Rosen CA, Carter KC, Moore PA;
PI Olsen HS, Shi Y, Young PE, Wei F, Brewer LA, Soppet DR;
PI Lafleur DW, Endress GA, Ebner R;
XX
DR WPI; 2000-062296/05.
DR N-PSDB; AAZ65277.
XX
PT New isolated human genes and the secreted polypeptides they encode,
PT useful for diagnosis and treatment of e.g. cancers, neurological
PT disorders, immune diseases, inflammation or blood disorders -
XX
PS Claim 11; Page 380-381; 475pp; English.
XX
CC AAZ65250 to AAZ65350 represent 97 isolated human secreted protein genes.
CC AAY76124 to AAY76223 are the secreted proteins encoded by the 97 human
CC genes. The gene encoding this protein was found to be on chromosome 3.
CC The genes and their corresponding secreted polypeptides are
CC useful for preventing, treating or ameliorating medical conditions,
CC e.g. by protein or gene therapy. Also pathological conditions can be
CC diagnosed by determining the amount of the new polypeptides in a sample
CC or by determining the presence of mutations in the new genes. Specific
CC uses are described for each of the 97 genes, based on which tissues they
CC are most highly expressed in, and include developing products for the
CC diagnosis or treatment of cancer, tumours, developmental abnormalities
CC and foetal deficiencies, blood disorders, diseases of the immune system,
CC autoimmune diseases, inflammation, allergies, Alzheimer's and cognitive
CC disorders, schizophrenia, arthritis, asthma, psoriasis, sepsis, skin
CC disorders, atherosclerosis, diabetes, cardiovascular disorders, kidney
CC disorders, digestive/endocrine disorders, infections and AIDS. The
CC polypeptides are also useful for identifying their binding partners.
CC The sequences shown in AAY76224 to AAY76424 represent fragments of the
CC secreted proteins.
XX
SQ Sequence 434 AA;

Query Match 83.8%; Score 1998; DB 21; Length 434;
Best Local Similarity 96.6%; Pred. No. 1.2e-139;
Matches 344; Conservative 6; Mismatches 6; Indels 0; Gaps 0;

```
Qy       6 PKGLVPAVLWGLSLFLNLPGPIWLQPSPPPQSSPPPQPHPCHTCRGLVDSFNKGLERTIR 65
           |:|||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       3 peglvpavlwglslflnlpgpiwlqpspppqssppppqphpchtcrglvdsfnkglertir 62

Qy      66 DNFGGGNTAWEEENLSKYKDSETRLVEVLEGVCSKSDFECHRLLELSEELVESWWFHKQQ 125
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      63 dnfgggntaweeenlskykdsetrlvevlegvcsksdfechrllelseelveswwfhkqq 122

Qy     126 EAPDLFQWLCSDSLKLCCPAGTFGPSCLPCPGGTERPCGGYGQCEGEGTRGGSGHCDCQA 185
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     123 eapdlfqwlcsdslklccpagtfgpsclpcpggterpcggygqcegegtrggsghcdcqa 182

Qy     186 GYGGEACGQCGLGYFEAERNASHLVCSACFGPCARCSGPEESNCLQCKKGWALHHLKCVD 245
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     183 gyggeacgqcglgyfeaernashlvcsacfgpcarcsgpeesnclqckkgwalhhlkcvd 242

Qy     246 IDECGTEGANCGADQFCVNTEGSYECRDCAKACLGCMGAGPGRCKKCSPGYQQVGSKCLD 305
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     243 idecgtegancgadqfcvntegsyecrdcakaclgcmgagpgrckkcspgyqqvgskcld 302

Qy     306 VDECETEVCPGENKQCENTEGGYRCICAEGYKQMEGICVKEQIPESAGFFSEMTED 361
           |||||||||||||||||||||||||||||||||||||||||| :    :::| :
Db     303 vdecetevcpgenkqcenteggyrcicaegykqmegicvkeqipgafpiltdltpe 358.
```

The amino acid sequence of Ruben's SEQ ID NO: 138 is 97% identical to the amino acid sequence of the polypeptide shown in Figure 40 (SEQ ID NO: 109) of the present application, lacking its associated signal peptide, as indicated below:

```
AAY76151
ID   AAY76151 standard; Protein; 434 AA.
XX
AC   AAY76151;
XX
DT   23-MAR-2000  (first entry)
XX
DE   Human secreted protein encoded by gene 28.
XX
KW   Human; secreted protein; cancer; tumour; developmental abnormality;
KW   foetal deficiency; blood disorder; immune system disorder; inflammation;
KW   autoimmune disease; allergy; Alzheimer's disease; cognitive disorder;
KW   schizophrenia; arthritis; asthma; psoriasis; sepsis; skin disorder;
KW   atherosclerosis; diabetes; cardiovascular disorder; kidney disorder;
KW   digestive disorder; endocrine disorder; infection; AIDS; leukaemia;
KW   therapy; chromosome 3.
XX
OS   Homo sapiens.
XX
PN   WO9958660-A1.
XX
PD   18-NOV-1999.
XX
PF   06-MAY-1999;   99WO-US09847.
XX
PR   12-MAY-1998;   98US-0085093.
PR   12-MAY-1998;   98US-0085094.
PR   12-MAY-1998;   98US-0085105.
PR   12-MAY-1998;   98US-0085180.
PR   18-MAY-1998;   98US-0085906.
PR   18-MAY-1998;   98US-0085920.
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PR 18-MAY-1998; 98US-0085921.
PR 18-MAY-1998; 98US-0085922.
PR 18-MAY-1998; 98US-0085923.
PR 18-MAY-1998; 98US-0085924.
PR 18-MAY-1998; 98US-0085928.
PR 18-MAY-1998; 98US-0085925.
PR 18-MAY-1998; 98US-0085927.
XX
PA (HUMA-) HUMAN GENOME SCI INC.
XX
PI Ruben SM, Florence K, Ni J, Rosen CA, Carter KC, Moore PA;
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PI Lafleur DW, Endress GA, Ebner R;
XX
DR WPI; 2000-062296/05.
DR N-PSDB; AAZ65277.
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PT New isolated human genes and the secreted polypeptides they encode,
PT useful for diagnosis and treatment of e.g. cancers, neurological
PT disorders, immune diseases, inflammation or blood disorders -
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CC AAZ65250 to AAZ65350 represent 97 isolated human secreted protein genes.
CC AAY76124 to AAY76223 are the secreted proteins encoded by the 97 human
CC genes. The gene encoding this protein was found to be on chromosome 3.
CC The genes and their corresponding secreted polypeptides are
CC useful for preventing, treating or ameliorating medical conditions,
CC e.g. by protein or gene therapy. Also pathological conditions can be
CC diagnosed by determining the amount of the new polypeptides in a sample
CC or by determining the presence of mutations in the new genes. Specific
CC uses are described for each of the 97 genes, based on which tissues they
CC are most highly expressed in, and include developing products for the
CC diagnosis or treatment of cancer, tumours, developmental abnormalities
CC and foetal deficiencies, blood disorders, diseases of the immune system,
CC autoimmune diseases, inflammation, allergies, Alzheimer's and cognitive
CC disorders, schizophrenia, arthritis, asthma, psoriasis, sepsis, skin
CC disorders, atherosclerosis, diabetes, cardiovascular disorders, kidney
CC disorders, digestive/endocrine disorders, infections and AIDS. The
CC polypeptides are also useful for identifying their binding partners.
CC The sequences shown in AAY76224 to AAY76424 represent fragments of the
CC secreted proteins.
XX
SQ Sequence 434 AA;

Query Match 84.3%; Score 1869; DB 21; Length 434;
Best Local Similarity 96.7%; Pred. No. 6.2e-133;
Matches 321; Conservative 5; Mismatches 6; Indels 0; Gaps 0;

```
Qy       1 QPSPPPQSSPPPQPHPCHTCRGLVDSFNKGLERTIRDNFGGGNTAWEEENLSKYKDSETR 60
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      27 qpspppqsspppqphpchtcrglvdsfnkglertirdnfgggntaweeenlskykdsetr 86

Qy      61 LVEVLEGVCSKSDFECHRLLELSEELVESWWFHKQQEAPDLFQWLCSDSLKLCCPAGTFG 120
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      87 lvevlegvcsksdfechrllelseelveswwfhkqqeapdlfqwlcsdslklccpagtfg 146

Qy     121 PSCLPCPGGTERPCGGYGQCEGEGTRGGSGHCDCQAGYGGEACGQCGLGYFEAERNASHL 180
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     147 psclpcpggterpcggygqcegegtrggsghcdcqagyggeacgqcglgyfeaernashl 206

Qy     181 VCSACFGPCARCSGPEESNCLQCKKGWALHHLKCVDIDECGTEGANCGADQFCVNTEGSY 240
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     207 vcsacfgpcarcsgpeesnclqckkgwalhhlkcvdidecgtegancgadqfcvntegsy 266

Qy     241 ECRDCAKACLGCMGAGPGRCKKCSPGYQQVGSKCLDVDECETEVCPGENKQCENTEGGYR 300
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                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    267 ecrdcakaclgcmgagpgrckkcspgyqqvgskcldvdecetevcpgenkqcenteggyr 326

Qy    301 CICAEGYKQMEGICVKEQIPESAGFFSEMTED 332
          |||||||||||||||||||  :    :::| :
Db    327 cicaegykqmegicvkeqipgafpiltdltpe 358,
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indicating that Ruben discloses a polypeptide at least 95% identical to the amino acid sequence of the polypeptide shown in Figure 40 (SEQ ID NO: 109) of the present application, to the amino acid sequence of the extracellular domain of the polypeptide shown in Figure 40 (SEQ ID NO: 109) of the present application, or to the amino acid sequence of the extracellular domain of the polypeptide shown in Figure 40 (SEQ ID NO: 109) of the present application, lacking its associated signal peptide. Ruben also discloses a fusion protein comprising SEQ ID NO: 138 and an epitope tag (page 197, line 8) or an Fc region of an immunoglobulin (page 197, lines 26-27).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The following rejection under 35 U.S.C. § 103 is made under the assumption that the effective filing date for the instantly claimed invention is February 22, 2000.

Claims 39-43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Koehrer (z10). Koehrer teaches a hypothetical protein that is at least 99% identical to SEQ ID NO: 109, as indicated below:

```
T08724
hypothetical protein DKFZp566D213.1 - human
C;Species: Homo sapiens (man)
C;Date: 11-Jun-1999 #sequence_revision 11-Jun-1999 #text_change 13-Aug-1999
C;Accession: T08724
R;Koehrer, K.; Beyer, A.; Mewes, H.W.; Gassenhuber, J.; Wiemann, S.
submitted to the Protein Sequence Database, May 1999
A;Reference number: Z16468
A;Accession: T08724
A;Molecule type: mRNA
A;Residues: 1-417 <KOE>
A;Cross-references: EMBL:AL050275
A;Experimental source: fetal kidney; clone DKFZp566D213
C;Genetics:
A;Note: DKFZp566D213.1

  Query Match             98.7%;  Score 2351;  DB 2;  Length 417;
  Best Local Similarity   99.5%;  Pred. No. 1.4e-150;
  Matches  415;  Conservative    0;  Mismatches    2;  Indels    0;  Gaps    0;

Qy       1 MAPWPPKGLVPAVLWGLSLFLNLPGPIWLQPSPPPQSSPPPQPHPCHTCRGLVDSFNKGL 60
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1 MAPWPPKGLVPAVLWGLSLFLNLPGPIWLQPSPPPQSSPPPQPHPCHTCRGLVDSFNKGL 60

Qy      61 ERTIRDNFGGGNTAWEEENLSKYKDSETRLVEVLEGVCSKSDFECHRLLELSEELVESWW 120
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      61 ERTIRDNFGGGNTAWEEENLSKYKDSETRLVEVLEGVCSKSDFECHRLLELSEELVESWW 120

Qy     121 FHKQQEAPDLFQWLCSDSLKLCCPAGTFGPSCLPCPGGTERPCGGYGQCEGEGTRGGSGH 180
           ||||| ||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     121 FHKQQGAPDLFQWLCSDSLKLCCPAGTFGPSCLPCPGGTERPCGGYGQCEGEGTRGGSGH 180

Qy     181 CDCQAGYGGEACGQCGLGYFEAERNASHLVCSACFGPCARCSGPEESNCLQCKKGWALHH 240
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     181 CDCQAGYGGEACGQCGLGYFEAERNASHLVCSACFGPCARCSGPEESNCLQCKKGWALHH 240

Qy     241 LKCVDIDECGTEGANCGADQFCVNTEGSYECRDCAKACLGCMGAGPGRCKKCSPGYQQVG 300
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     241 LKCVDIDECGTEGANCGADQFCVNTEGSYECRDCAKACLGCMGAGPGRCKKCSPGYQQVG 300

Qy     301 SKCLDVDECETEVCPGENKQCENTEGGYRCICAEGYKQMEGICVKEQIPESAGFFSEMTE 360
           |||||||||||||||||||||||||||||||| ||||||||||||||||||||||||||
```

```
Db    301 SKCLDVDECETEVCPGENKQCENTEGGYRCICAEGCKQMEGICVKEQIPESAGFFSEMTE 360

Qy    361 DELVVLQQMFFGIIICALATLAAKGDLVFTAIFIGAVAAMTGYWLSERSDRVLEGFI 417
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    361 DELVVLQQMFFGIIICALATLAAKGDLVFTAIFIGAVAAMTGYWLSERSDRVLEGFI 417;
```

is at least 99% identical to the amino acid sequence of the polypeptide shown in Figure 40 (SEQ ID NO: 109), lacking its associated signal peptide, as indicated below:

```
T08724
hypothetical protein DKFZp566D213.1 - human
C;Species: Homo sapiens (man)
C;Date: 11-Jun-1999 #sequence_revision 11-Jun-1999 #text_change 13-Aug-1999
C;Accession: T08724
R;Koehrer, K.; Beyer, A.; Mewes, H.W.; Gassenhuber, J.; Wiemann, S.
submitted to the Protein Sequence Database, May 1999
A;Reference number: Z16468
A;Accession: T08724
A;Molecule type: mRNA
A;Residues: 1-417 <KOE>
A;Cross-references: EMBL:AL050275
A;Experimental source: fetal kidney; clone DKFZp566D213
C;Genetics:
A;Note: DKFZp566D213.1

 Query Match           98.6%;  Score 2184;  DB 2;  Length 417;
 Best Local Similarity 99.5%;  Pred. No. 3.5e-141;
 Matches  386;  Conservative    0;  Mismatches    2;  Indels    0;  Gaps    0;

Qy      1 QPSPPPQSSPPPQPHPCHTCRGLVDSFNKGLERTIRDNFGGGNTAWEEENLSKYKDSETR 60
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     30 QPSPPPQSSPPPQPHPCHTCRGLVDSFNKGLERTIRDNFGGGNTAWEEENLSKYKDSETR 89

Qy     61 LVEVLEGVCSKSDFECHRLLELSEELVESWWFHKQQEAPDLFQWLCSDSLKLCCPAGTFG 120
          ||||||||||||||||||||||||||||||||| ||||||||||||||||||||||||||
Db     90 LVEVLEGVCSKSDFECHRLLELSEELVESWWFHKQQGAPDLFQWLCSDSLKLCCPAGTFG 149

Qy    121 PSCLPCPGGTERPCGGYGQCEGEGTRGGSGHCDCQAGYGGEACGQCGLGYFEAERNASHL 180
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    150 PSCLPCPGGTERPCGGYGQCEGEGTRGGSGHCDCQAGYGGEACGQCGLGYFEAERNASHL 209

Qy    181 VCSACFGPCARCSGPEESNCLQCKKGWALHHLKCVDIDECGTEGANCGADQFCVNTEGSY 240
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    210 VCSACFGPCARCSGPEESNCLQCKKGWALHHLKCVDIDECGTEGANCGADQFCVNTEGSY 269

Qy    241 ECRDCAKACLGCMGAGPGRCKKCSPGYQQVGSKCLDVDECETEVCPGENKQCENTEGGYR 300
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    270 ECRDCAKACLGCMGAGPGRCKKCSPGYQQVGSKCLDVDECETEVCPGENKQCENTEGGYR 329

Qy    301 CICAEGYKQMEGICVKEQIPESAGFFSEMTEDELVVLQQMFFGIIICALATLAAKGDLVF 360
          |||||| ||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db    330 CICAEGCKQMEGICVKEQIPESAGFFSEMTEDELVVLQQMFFGIIICALATLAAKGDLVF 389

Qy    361 TAIFIGAVAAMTGYWLSERSDRVLEGFI 388
          ||||||||||||||||||||||||||||
Db    390 TAIFIGAVAAMTGYWLSERSDRVLEGFI 417; and,
```

is at least 99% identical to the amino acid sequence of the extracellular domain of the polypeptide shown in Figure 40 (SEQ ID NO: 109), or to the amino acid sequence of the extracellular domain of the polypeptide shown in Figure 40 (SEQ ID NO: 109), lacking its associated signal peptide, as indicated below:

```
T08724
hypothetical protein DKFZp566D213.1 - human
C;Species: Homo sapiens (man)
C;Date: 11-Jun-1999 #sequence_revision 11-Jun-1999 #text_change 13-Aug-1999
C;Accession: T08724
R;Koehrer, K.; Beyer, A.; Mewes, H.W.; Gassenhuber, J.; Wiemann, S.
submitted to the Protein Sequence Database, May 1999
A;Reference number: Z16468
A;Accession: T08724
A;Molecule type: mRNA
A;Residues: 1-417 <KOE>
A;Cross-references: EMBL:AL050275
A;Experimental source: fetal kidney; clone DKFZp566D213
C;Genetics:
A;Note: DKFZp566D213.1

  Query Match           99.2%;  Score 1956;  DB 2;  Length 417;
  Best Local Similarity 99.4%;  Pred. No. 2.8e-124;
  Matches  340;  Conservative    0;  Mismatches    2;  Indels    0;  Gaps    0;

Qy       1 QPSPPPQSSPPPQPHPCHTCRGLVDSFNKGLERTIRDNFGGGNTAWEEENLSKYKDSETR 60
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      30 QPSPPPQSSPPPQPHPCHTCRGLVDSFNKGLERTIRDNFGGGNTAWEEENLSKYKDSETR 89

Qy      61 LVEVLEGVCSKSDFECHRLLELSEELVESWWFHKQQEAPDLFQWLCSDSLKLCCPAGTFG 120
           |||||||||||||||||||||||||||||||| ||||||||||||||||||||||||||||
Db      90 LVEVLEGVCSKSDFECHRLLELSEELVESWWFHKQQGAPDLFQWLCSDSLKLCCPAGTFG 149

Qy     121 PSCLPCPGGTERPCGGYGQCEGEGTRGGSGHCDCQAGYGGEACGQCGLGYFEAERNASHL 180
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     150 PSCLPCPGGTERPCGGYGQCEGEGTRGGSGHCDCQAGYGGEACGQCGLGYFEAERNASHL 209

Qy     181 VCSACFGPCARCSGPEESNCLQCKKGWALHHLKCVDIDECGTEGANCGADQFCVNTEGSY 240
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     210 VCSACFGPCARCSGPEESNCLQCKKGWALHHLKCVDIDECGTEGANCGADQFCVNTEGSY 269

Qy     241 ECRDCAKACLGCMGAGPGRCKKCSPGYQQVGSKCLDVDECETEVCPGENKQCENTEGGYR 300
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     270 ECRDCAKACLGCMGAGPGRCKKCSPGYQQVGSKCLDVDECETEVCPGENKQCENTEGGYR 329

Qy     301 CICAEGYKQMEGICVKEQIPESAGFFSEMTEDELVVLQQMFF 342
           |||||| |||||||||||||||||||||||||||||||||||
Db     330 CICAEGCKQMEGICVKEQIPESAGFFSEMTEDELVVLQQMFF 371.
```

To the extent that the amino acid sequence of the polypeptide encoded by the full-length coding sequence of the cDNA deposited under ATCC accession number 209385 is the amino acid sequence of SEQ ID NO: 109, then the above also applies to this claim embodiment.

Koehrer does not teach an isolated protein. However, it would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to recombinantly produce and isolate the hypothetical protein, with a reasonable expectation of success. One of ordinary skill in the art would be motivated to make this modification, in order to study the function of the protein, or in order to make antibodies to the protein so that expression of the hypothetical protein could be assessed or confirmed. The invention is prima facie obvious over the prior art.

Conclusion

Claims 44-49 are allowable.

ANY INQUIRY CONCERNING THIS COMMUNICATION OR EARLIER COMMUNICATIONS FROM THE EXAMINER SHOULD BE DIRECTED TO DAVID S. ROMEO WHOSE TELEPHONE NUMBER IS (703) 305-4050. THE EXAMINER CAN NORMALLY BE REACHED ON MONDAY THROUGH FRIDAY FROM 7:30 A.M. TO 4:00 P.M.

IF ATTEMPTS TO REACH THE EXAMINER BY TELEPHONE ARE UNSUCCESSFUL, THE EXAMINER'S SUPERVISOR, GARY KUNZ, CAN BE REACHED ON (703) 308-4623.

IF SUBMITTING OFFICIAL CORRESPONDENCE BY FAX, APPLICANTS ARE ENCOURAGED TO SUBMIT OFFICIAL CORRESPONDENCE TO THE FOLLOWING TC 1600 BEFORE AND AFTER FINAL RIGHTFAX NUMBERS:

BEFORE FINAL (703) 872-9306
AFTER FINAL (703) 872-9307

IN ADDITION TO THE OFFICIAL RIGHTFAX NUMBERS ABOVE, THE TC 1600 FAX CENTER HAS THE FOLLOWING OFFICIAL FAX NUMBERS: (703) 305-3592, (703) 308-4242 AND (703) 305-3014.

CUSTOMERS ARE ALSO ADVISED TO USE CERTIFICATE OF FACSIMILE PROCEDURES WHEN SUBMITTING A REPLY TO A NON-FINAL OR FINAL OFFICE ACTION BY FACSIMILE (SEE 37 CFR 1.6 AND 1.8).

FAXED DRAFT OR INFORMAL COMMUNICATIONS SHOULD BE DIRECTED TO THE EXAMINER AT (703) 308-0294.

ANY INQUIRY OF A GENERAL NATURE OR RELATING TO THE STATUS OF THIS APPLICATION OR PROCEEDING SHOULD BE DIRECTED TO THE GROUP RECEPTIONIST WHOSE TELEPHONE NUMBER IS (703) 308-0196.

David Romeo

DAVID ROMEO
PRIMARY EXAMINER
ART UNIT 1647

DSR
SEPTEMBER 30, 2002